## WHAT IS CLAIMED IS:

- 1. A method of treating a subject diagnosed as having a lysosomal storage disease comprising administering a gene therapy vector encoding a lysosomal hydrolase under the control of at least one tissue specific regulatory element and administering:
  - (a) an exogenously produced natural or recombinant lysosomal hydrolase;
  - (b) a small molecule capable of treating a lysosomal storage disease, or
  - (c) both (a) and (b), such that the lysosomal storage disease is treated.
- 2. The method of claim 1, where the gene therapy vector encoding a lysosomal hydrolase under the control of a tissue specific regulatory element is administered before the exogenously produced natural or recombinant lysosomal hydrolase or the small molecule capable of treating a lysosomal storage disease.
- 3. The method of claim 1, where the tissue specific regulatory element is chosen from at least one of a tissue specific promoter and a tissue specific enhancer.
- 4. The method of claim 1, where administering the gene therapy vector encoding a lysosomal hydrolase induces immunological tolerance to the lysosomal hydrolase.
- 5. The method of claim 1, where administration of the gene therapy vector encoding a lysosomal hydrolase under the control of a tissue specific

promoter is followed by administration of an exogenously produced natural or recombinant lysosomal hydrolase.

- 6. The method of claim 5, where the amount of the exogenously produced natural or recombinant lysosomal hydrolase administered to the subject is less than the amount administered to treat a subject with a lysosomal storage disease that has not been administered a gene therapy vector encoding a lysosomal hydrolase or has been administered a gene therapy vector without a tissue specific promoter controlling expression of the lysosomal hydrolase.
- 7. The method of claim 1, where the lysosomal storage disease is Fabry disease.
- 8. The method of claim 7, where the treatment results in a decrease in GL-3 in the subject compared to the GL-3 level in the subject before treatment.
- 9. The method of claim 7, where the lysosomal hydrolase is  $\alpha$ -galactosidase A.
- 10. The method of claim 1, where the lysosomal storage disease is Pompe disease.
- 11. The method of claim 10, where the treatment results in a decrease in glycogen in the subject compared to the glycogen level in the subject before treatment.
- 12. The method of claim 10, where the lysosomal hydrolase is  $\alpha$ -glucosidase.
  - 13. The method of claim 1, where the gene therapy vector is a viral vector.

- 14. The method of claim 11, where the viral vector is chosen from AAV1, AAV2, AAV5, AAV7 and AAV8.
- 15. The method of claim 1, where the tissue specific regulatory element is a liver specific promoter.
- 16. The method of claim 15, where the liver specific promoter is a human serum albumin promoter.
- 17. The method of claim 1, where tissue specific regulatory element is a tissue specific enhancer.
- 18. The method of claim 17, where the tissue specific enhancer is a human prothrombin enhancer.
- 19. The method of claim 1, where the small molecule capable of treating a lysosomal storage disease is chosen from deoxynojirimycin, N-propyldeoxynojirimycin, N-butyldeoxynojirimycin, N-butyldeoxynojirimycin, N-pentlydeoxynojirimycin, N-pentlydeoxynojirimycin, N-pentlydeoxynojirimycin, N-pentlydeoxynojirimycin, N-pentlyloeoxynojirimycin, N-(5-cholesteroxypentyl)-deoxynojirimycin, N-(4-adamantanemethanylcarboxy-1-oxo)-deoxynojirimycin, N-(4-adamantanylcarboxy-1-oxo)-deoxynojirimycin, N-(4-phenantrylcarboxy-1-oxo)-deoxynojirimycin, N-(4-cholesterylcarboxy-1-oxo)-deoxynojirimycin, or N-(4-b-cholestanylcarboxy-1-oxo)-deoxynojirimycin, D-threo-1-phenyl-2-palmitoylamino-3-pyrrolidino-1-propanol (P4), D-threo-4'-hydroxy-1-phenyl-2-palmitoylamino-3-pyrrolidino-1-propanol (4'-hydroxy-P4), D-threo-1-(3',4'-trimethylenedioxy)phenyl-2-palmitoylamino-3-pyrrolidino-1-propanol (methylenedioxy-P4), D-threo-1-(3',4'-trimethylenedioxy-P4), D-threo-1-(3',4'-trimethylened

- P4) and D-threo-1-(3',4'-ethylenedioxy)phenyl-2-palmitoylamino-3-pyrrolidino-1-propanol (ethylenedioxy-P4 or D-t-et-P4).
- 20. A method of treating a subject diagnosed as having Fabry disease comprising administering a gene therapy vector encoding α-galactosidase A under the control of a human albumin promoter and 2 copies of a human prothrombin enhancer and administering:
  - (a) an exogenously produced natural or recombinant  $\alpha$ -galactosidase A;
    - (b) a small molecule capable of treating Fabry disease, or
    - (c) both (a) and (b),

such that the Fabry disease is treated.

- 21. The method of claim 20, where the gene therapy vector encoding  $\alpha$ -galactosidase A under the control of a human albumin promoter and 2 copies of a human prothrombin enhancer is administered before the exogenously produced natural or recombinant  $\alpha$ -galactosidase A or a small molecule capable of treating Fabry disease.
- 22. A method of treating a subject diagnosed as having Pompe disease comprising first administering a gene therapy vector encoding α-glucosidase under the control of a liver specific promoter and optionally, at least one copy of a tissue specific enhancer followed by administration of:
  - (a) an exogenously produced natural or recombinant  $\alpha$ -glucosidase;
  - (b) a small molecule capable of treating Pompe disease, or
  - (c) both (a) and (b),

such that the Pompe disease is treated.

- 23. A composition useful for treating a lysosomal storage disease comprising a gene therapy vector encoding a lysosomal hydrolase under the control of a tissue specific regulatory element and (a) an exogenously produced natural or recombinant lysosomal hydrolase; (b) a small molecule capable of treating a lysosomal storage disease or (c) both (a) and (b).
- 24. The composition of claim 23, where the gene therapy vector encoding a lysosomal hydrolase encodes α-galactosidase A.
- 25. The composition of claim 23, where the gene therapy vector encoding a lysosomal hydrolase encodes  $\alpha$ -glucosidase.
- 26. The composition of claim 23, where the gene therapy vector is a viral vector.
- 27. The composition of claim 26, where the viral vector is chosen from AAV1, AAV2, AAV5, AAV7 and AAV8.
- 28. The composition of claim 23, where the exogenously produced natural or recombinant lysosomal hydrolase is chosen from  $\alpha$ -galactosidase A and  $\alpha$ -glucosidase.
- 29. The composition of claim 23, where the tissue specific regulatory element is a liver specific promoter.
- 30. The composition of claim 29, where the liver specific promoter is an albumin promoter.
- 31. The composition of claim 23, where the tissue specific regulatory element is a tissue specific enhancer.

- 32. The composition of claim 31, where the tissue specific enhancer is a human prothrombin enhancer.
- 33. The composition of claim 23, where the small molecule capable of treating a lysosomal storage disease is chosen from deoxynojirimycin, Npropyldeoxynojirimycin, N-butyldeoxynojirimycin, N-butyldeoxygalactonojirimycin, Npentlydeoxynojirimycin, N-heptyldeoxynojirimycin, N-pentanoyldeoxynojirimycin, N-(5-adamantane-1-ylmethoxy)pentyl)-deoxynojirimycin, N-(5-cholesteroxypentyl)deoxynojirimycin, N-(4-adamantanemethanylcarboxy-1-oxo)-deoxynojirimycin, N-(4adamantanylcarboxy-1-oxo)-deoxynojirimycin, N-(4-phenantrylcarboxy-1-oxo)deoxynojirimycin, N-(4-cholesterylcarboxy-1-oxo)-deoxynojirimycin, or N-(4-bcholestanylcarboxy-1-oxo)-deoxynojirimycin, D-threo-1-phenyl-2-palmitoylamino-3pyrrolidino-1-propanol (P4), D-threo-4'-hydroxy-1-phenyl-2-palmitoylamino-3pyrrolidino-1-propanol (4'-hydroxy-P4), D-threo-1-(3',4'-trimethylenedioxy)phenyl-2palmitoylamino-3-pyrrolidino-1-propanol (trimethylenedioxy-P4), D-threo-1-(3',4'methylenedioxy)phenyl-2-palmitoylamino-3-pyrrolidino-1-propanol (methylenedioxy-P4) and D-threo-1-(3',4'-ethylenedioxy)phenyl-2-palmitoylamino-3-pyrrolidino-1propanol (ethylenedioxy-P4 or D-t-et-P4).
- 34. A composition useful for treating Fabry disease comprising a gene therapy vector encoding α-galactosidase A under the control of a human albumin promoter and 2 copies of a human prothrombin enhancer and:
  - (a) an exogenously produced natural or recombinant  $\alpha$ -galactosidase A;
    - (b) a small molecule capable of treating Fabry disease, or

- (c) both (a) and (b).
- 35. A composition useful for treating Pompe disease comprising a gene therapy vector encoding  $\alpha$ -glucosidase under the control of a liver specific promoter and optionally at least one tissue specific enhancer and:
  - a) an exogenously produced natural or recombinant α-glucosidase;
  - b) a small molecule capable of treating Pompe disease or
  - (c) both (a) and (b).